

Availability, affordability, and quality of essential anti-seizure medication in Cambodia

Noudy Sengxeu^{1,2}  | Chanraksmeay Aon³ | Hanh Dufat⁴ | Farid Boumediene¹ | Samleng Chan³ | Sina Ros³ | Pierre-Marie Preux¹ | Voa Ratsimbazafy^{1,5} | Jeremy Jost^{1,5} 

¹INSERM, Univ. Limoges, CHU Limoges, IRD, U1094 Tropical Neuroepidemiology, Institute of Epidemiology and Tropical Neurology, GEIST, Limoges, France

²Faculty of Pharmacy, University of Health Sciences, Vientiane, Lao PDR

³Cambodian Society of Neurology, Calmette Hospital, Phnom Penh, Cambodia

⁴Natural Products, Analysis and Synthesis, CiTCoM (Cibles Thérapeutiques et Conception de Médicaments)-UMR 8038 CNRS/Université de Paris, Faculty of Health-Pharmacie, Université de Paris, Paris, France

⁵Department of Pharmacy, CHU Limoges, Limoges, France

Correspondence

Sengxeu Noudy, Institute of Epidemiology and Tropical Neurology, 2 rue du Docteur Marcland 87025 Limoges, France; Faculty of pharmacy, University of health sciences, Vientiane, Lao PDR.
Email: no.dy1990@hotmail.com

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Abstract

Objective: Epilepsy is a major neurological disorder that requires long-term medical treatment. Once epilepsy is diagnosed, people with epilepsy face many difficulties in accessing treatment (treatment gap). Our objective was to assess the situation regarding the availability, price, affordability, and quality of anti-seizure medication (ASM), which are major determinants of access to treatment.

Method: A cross-sectional study was performed in provincial/district hospitals and private pharmacies in urban and rural areas in Cambodia. Data on ASM availability and price were obtained through drug suppliers. Affordability was estimated as the number of day wages the lowest-paid government employee must work to purchase a monthly treatment. Samples of ASM were collected, and the quality of ASM was assessed through Medicine Quality Assessment Reporting Guidelines.

Results: Out of 138 outlets visited, only 72 outlets (52.2% [95% CI 43.5-60.7]) had at least one ASM available. Phenobarbital 100 mg was the most available (35.5%), followed by carbamazepine 200 mg (21.7%), phenobarbital 50 mg (11.6%), sodium valproate 500 mg (9.4%), and phenytoin 100 mg (9.4%). In provincial/district hospitals, ASM was provided free of charge. In private pharmacies, affordability for phenobarbital 50 mg and 100 mg was the best, with 0.6 and 0.5 days, respectively, compared to phenytoin 100 mg (1.8 days), and other ASM. No counterfeit ASM was found in this study. Phenytoin sample presented the worst quality (33.0%) compared to carbamazepine (27.8%), and other ASM.

Significance: A lack of access to affordable and effective ASM due to low availability and poor quality of ASM was identified. Our research highlights the need for future policy efforts to ensure the quality of ASM and improve their availability. This can be achieved by involving the calculation of their annual needs for these drugs and increasing the national production of ASM.

KEY WORDS

accessibility, anti-seizure medication, Asia, epilepsy, treatment gap

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1 | INTRODUCTION

Epilepsy is a major neurological disorder that requires long-term medical treatment.¹ It affects people of all ages, gender, race, and income levels.² The mortality rate of people with epilepsy (PWE) was 2 to 3 times higher than the general population, but the disease is often wrongly considered a nonfatal, nondisabling condition.³ The majority of PWE can be efficiently treated by cost-effective, affordable anti-seizure medication (ASM). Unfortunately, once epilepsy is diagnosed, patients in many low- and middle-income countries (LMICs) face difficulties in accessing treatment, with the treatment gap estimated to be around 75%.⁴⁻⁶ The price of medicines, availability, and affordability are major determinants of access to treatment, and it is a matter of concern for both patients and governments. However, studies and routinely collected data on medicine availability and prices are still scarce, especially for the treatment of epilepsy.⁷ A recent study in Lao PDR demonstrated the low availability of all essential ASM.⁸ Another study in Madagascar shows that the least affordable ASM (sodium valproate) was the most available instead of phenobarbital. In the same study, original brands were more available than generic formulations.⁹ Furthermore, poor-quality or counterfeit drugs, inappropriate storage conditions, and poor-quality control during manufacturing are another concern.⁷ A high poor quality (65%) of major ASM has been reported in Vietnam.¹⁰ Similarly, in Lao PDR, approximately half of the sample of phenobarbital collected in 2018, which was the most available and affordable ASM, was of poor quality.⁸ Besides, a study performed in sub-Saharan Africa shown that tropical environmental factors (temperature, relative humidity, light) have a strong influence on the quality of carbamazepine, phenytoin, and sodium valproate tablets.¹¹

Cambodia, a Southeast Asian country, has a population of 14 million people. Almost two-thirds of the population lives in rural areas and 36% of the population lives below the poverty line.¹² In Cambodia's public sector, drug distribution is centralized. However, the public health system is still experiencing drug shortages and storage conditions of medicines at all levels of distribution need to be improved.¹³ The private sector is an important provider of health services and has grown rapidly.¹⁴ Cambodia has several local manufacturing companies. Although there have been significant achievements in the pharmaceutical sector, the production techniques of local manufacturers still do not comply with Good Manufacturing Practice.¹³ The prevalence of epilepsy in Cambodia is 5.8/1000 with a treatment gap of 65.8% in 2011.^{15, 16} Epilepsy adds to the burden of mental health in Cambodia but mental health expenditures from the Ministry of Health are not available nor are expenditures from psychiatric hospitals. Since 2013, the Cambodian Epilepsy

Key points

- Limited access to anti-seizure medication was mainly due to availability and quality issues.
- Overall availability of ASM in all supply chains was significantly (<36.0%) below the WHO-recommended threshold
- A proportion of 23.9% of the sample was of poor quality and concerned all types of ASM.
- A significant difference in substandard samples was observed across healthcare sectors (68.8% in private vs 31.3% in public; $P = .016$).

Association and the Cambodian Neurology Association have been established. Cambodia has about 7 neurologists and 1 neuro-rehabilitation specialist, and various healthcare providers (health center staff, general practitioners, and medical students).¹⁷

Eight molecules of ASM (carbamazepine, phenobarbital, phenytoin, sodium valproate, diazepam, gabapentin, lamotrigine, and magnesium sulfate) are registered in the essential drug list of Cambodia (9th edition, 2018) which are provided free of charge in public healthcare facilities.¹⁸ However, epilepsy has the highest number of treatment dropouts, more than any other neuropsychiatric disorder.¹⁶ A study in Cambodia performed in 2012 has shown that only a third of PWE (34.3%) were treated by ASM, and a high proportion of patients (43%) were not on any treatment.¹⁵ No price regulation system in Cambodia leaves manufacturers, wholesalers, and retailers free in setting the selling price.¹⁹ This system may result in an important source of out-of-pocket expenditures for patients with disparity on the territory.²⁰ A study performed in 2010 has shown that insufficient regulation in Cambodia provides opportunities for counterfeit and/or substandard medicines to enter the pharmaceutical market through unauthorized channels.²¹ Many drug retailers (pharmacy, drug depot, ...), which are the first and one of the most regular points of contact of patients with the healthcare system, are often run by nonprofessionals.²² In many situations, storage conditions are inappropriate such as plastic containers without any desiccators (static adsorption of moisture in a closed environment), bottles without caps, no air-conditioning in the storage room, or operating intermittently.²³ Furthermore, a recent study performed in Lao PDR and Cambodia has shown a lack of knowledge about epilepsy and the appropriate use of ASM among pharmacy-dispensing workers.²² All of these aspects are avoidable determinants of the treatment gap. Until

present, there are no published data on the availability, affordability, and quality of antiepileptic drugs in Cambodia. Our objective was to assess these determinants of accessibility to ASM at the end of the supply chain in urban and rural areas in Cambodia.

2 | METHODOLOGY

2.1 | Study area

The study design was a cross-sectional qualitative study. Random sampling outlets were conducted from June to July 2018 in Cambodia. This study was carried out in 3 provinces included Phnom Penh, Kampong cham province, and Kampot province (share border with Vietnam) (Figure 1). These provinces account for 27.6% of the total population (Cambodia census population survey 2013 final report²⁴). The total number of expected PWE in these provinces was 23 540 (calculated based on the prevalence of 5.8/1000). Then, in each province, the district with the highest population density was selected as the urban district and the district that had the lowest population density was selected as the rural one.

2.2 | Medicine inclusion criteria

This study included solid oral pharmaceutical forms (tablet/capsule) of four ASM (phenytoin, phenobarbital, carbamazepine, and sodium valproate) that are listed on the 20th WHO essential medicines list.

2.3 | Sample size

In Cambodia, healthcare facilities were delivered in two sectors: public and private. The public sector was organized around the Operational Health District (OD) and divided into provincial hospitals, district hospitals, and health centers. The private sector was composed of private hospitals, clinics, and pharmacies (level I run by pharmacists; level II run by pharmacist assistants, level III run by nurses).^{23, 25} We included provincial hospitals, district hospitals, and all types of pharmacies (I, II, III). Private hospitals and clinics were not included because we did not obtain authorization from the ministry of health. Similarly, primary health centers in Cambodia provided a minimum package of activities (MPA) consisting of preventive services and basic curative care, and they were not included in the present study.²⁶ After communicating with the district health office in each district, we obtained lists of registered public and private health facilities within the area. At the time of data collection, there were a total of 202 outlets registered in the 6 districts selected: 6 (2.9%) outlets were of the public sector (2 provincial hospitals, 4 district hospitals), and 196 (97.0%) outlets were of the private pharmacies. Figure 2 presents the flowchart of the sampled outlets. Data on availability and price of ASM were collected from all provincial hospitals, and district hospitals presented in both urban and rural districts. Random sampling was performed to select 50% of private pharmacies (I, II, III) in the urban district. In the rural district, all private pharmacies were included.

For data collection, availability and affordability endpoints, and data analysis were adapted from those used in another project performed in Lao PDR and published in 2020.⁸

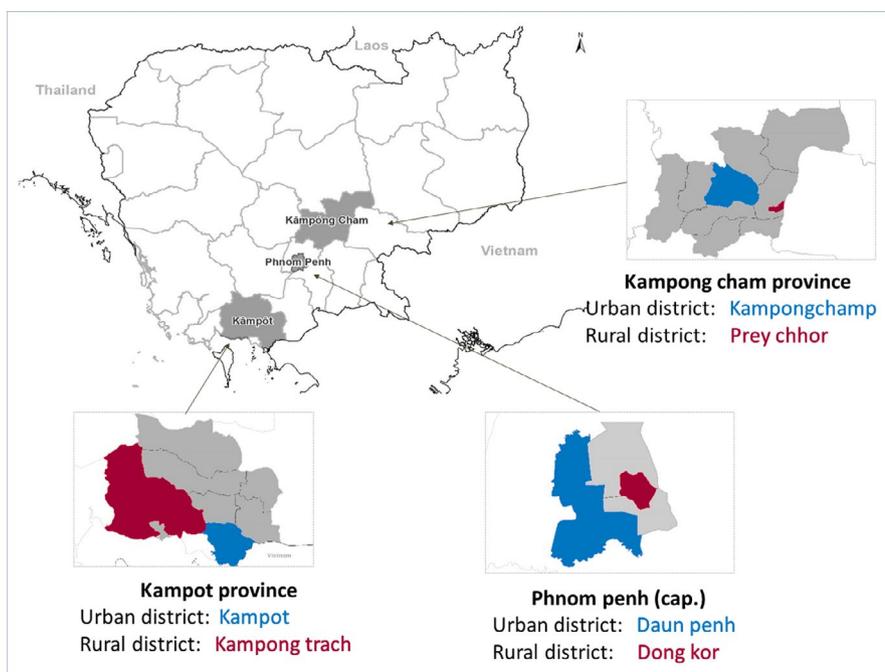
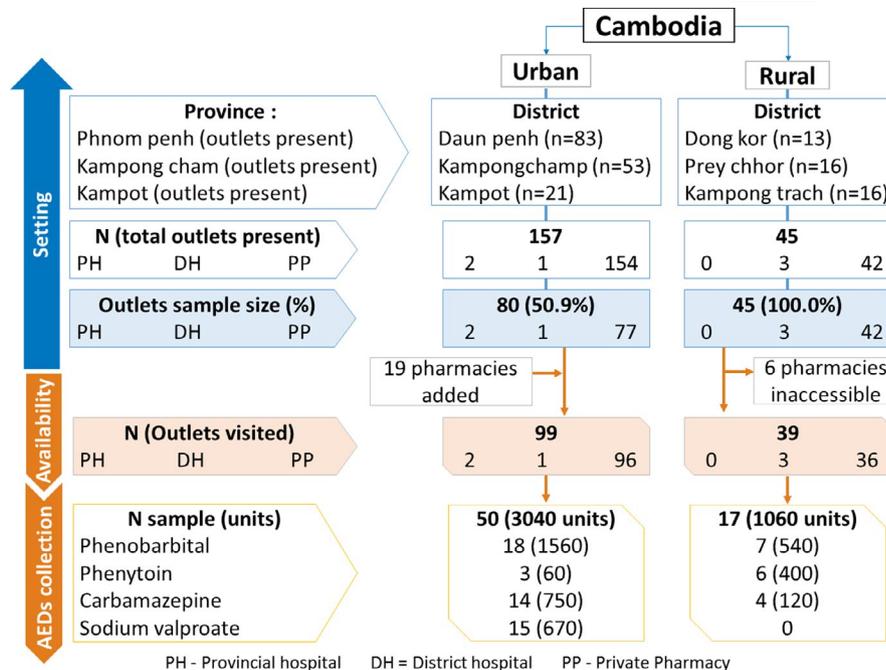


FIGURE 1 Study area

FIGURE 2 Sampling flowchart



2.4 | Data collection

Anti-seizure medication availability, strength, cost, and country of manufacture were obtained from the head of the pharmacy service in the public sector. In the private sector, investigators gathered information by acting as a patient, showing a handwritten prescription of ASM with the International Non-proprietary Name (never the brand name), and then asking questions such as "I would like to buy these drugs - Are these drugs available? If so, what strength? How much does it cost? And what is the country of manufacture?"

2.5 | Endpoints

The availability was expressed as a percentage by strength per molecule. To express the availability, the following ranges were used: very low: < 30%; low: 30%–49%; fairly high: 50%–80%; high: >80%.²⁷ Pricing information was expressed as median price ratios (MPRs) based on the WHO/HAI methodology.²⁸ The MPR was calculated by median unit price, compared with International Reference Prices (IRPs). An MPR of 1.0 means that the local price is equivalent to the IRP. Treatment affordability was estimated as the number of day wages the lowest-paid government employee needed to purchase a monthly treatment. But due to the nonpublication of the minimum wage of lowest-paid government worker, we used the garment factory workers' wage (US\$100 per month in 2014)²⁹ to express affordability, which is one of the lowest wage levels in the country. The Defined Daily Dose (DDD) of individual medicines³⁰ was used to estimate monthly treatment costs of ASM.

2.6 | Quality of ASM

Endpoints, sampling methodology, and analytical testing were adapted from those used in another project performed in sub-Saharan Africa and published in 2018.¹¹ A degree of the quality scale was designed based on the type of issue(s) observed (active ingredient assay, impurities screening, pharmacotechnical features) (Figure S1).

2.7 | Data analysis and statistics

Statistical analyses were performed using SPSS version 23.0. Proportion, means, standard deviations, and 95% confidence intervals (CIs) were used for the descriptive analysis. Chi-square and Fisher's exact tests were performed for comparative analysis. Multinomial logistic regression was performed to identify the association between the independent variables (storage conditions including presence or absence of air-conditioning, exposure to light or wind; presence or absence of packaging; healthcare sector; study area; local or imported ASM) and the dependent variable (quality of ASM). Only variables with a *P*-value <.25 after univariate analysis were entered into a multivariate logistic regression model using the backward stepwise exclusion method.

2.8 | Ethical approval

Ethics approval for this study was obtained from the National Ethics committee for Health Research, Ministry of Health of Cambodia (reference No.12/NECHR).

3 | RESULTS

3.1 | Sampling

Of the 125 randomized outlets, six were inaccessible due to flooding in Kampong champ province on the day of data collection. Nineteen private pharmacies within a kilometer radius of provincial/district hospitals were added, due to their proximity to health centers able to diagnose epilepsy. Finally, 138 outlets were included in this study corresponding to a proportion of 68.3% of the total number of outlets present in the study area (2 provincial hospitals, 3 district hospitals, and 132 private pharmacies).

3.2 | Availability

The overall ASM availability was 52.2% (72/138 outlets) (95% confidence interval [CI] 43.5-60.7). Availability in the public sector was 100.0% (6/6 outlets) and 50.0% (66/132 outlets) in the private sector, $P = .029$. Availability in the urban area was 57.6% (57/99 outlets) and 38.5% (15/39 outlets) in rural areas; no statistical difference was observed. The availability of ASM within healthcare facilities is detailed in Figure 3.

3.2.1 | Choice of ASM per outlets

Nature and the number of molecules available varied. Among outlets where ASM was available in the urban area ($n = 57$), 32.3% had only 1 type ASM, 13.1% had two different ASM, 6.1% had three different ASM, and 6.1% had all the four

ASM considered in this study. Among outlets where ASM was available in the rural area ($n = 15$), 30.8% had only 1 type ASM, 2.6% had two different ASM, 5.1% had three different ASM, and no outlets had all the four ASM.

3.2.2 | Availability per ASM

In provincial/district hospitals, only phenobarbital 50 mg, phenytoin 100 mg, and carbamazepine 200 mg were available. Overall, phenobarbital 100 mg was the most available in 49 outlets (35.5% [95% CI 26.7-44.1]), followed by carbamazepine 200 mg in 30 outlets (21.7% [95% CI 15.2-29.6]), phenobarbital 50 mg in 16 outlets (11.6% [95% CI 6.8-18.1]), sodium valproate 500 mg in 13 outlets (9.4% [95% CI 5.1-15.6]), and phenytoin 100 mg in 13 outlets (9.4% [95% CI 5.1-15.6]). Other strength of sodium valproate (200 mg) and carbamazepine (400 mg) was also available in 8 (5.8% [95% CI 2.5-11.1]) and 1 outlet (0.7% [95% CI 0.01-4.0]), respectively. The availability of carbamazepine 200 mg was higher in an urban area than in rural areas (26.3% vs. 10.3%, $P = .042$). In contrast, the availability of other ASM was not significantly different between urban and rural areas. Another important finding was the absence of sodium valproate at any dose in the rural area.

3.2.3 | Origins of ASM available

Phenobarbital 50 and 100 mg sold in the private sectors were produced locally from three Cambodian pharmaceutical manufactories, while imported phenobarbital 50 mg from India were sold in the public sectors. Carbamazepine 200 mg

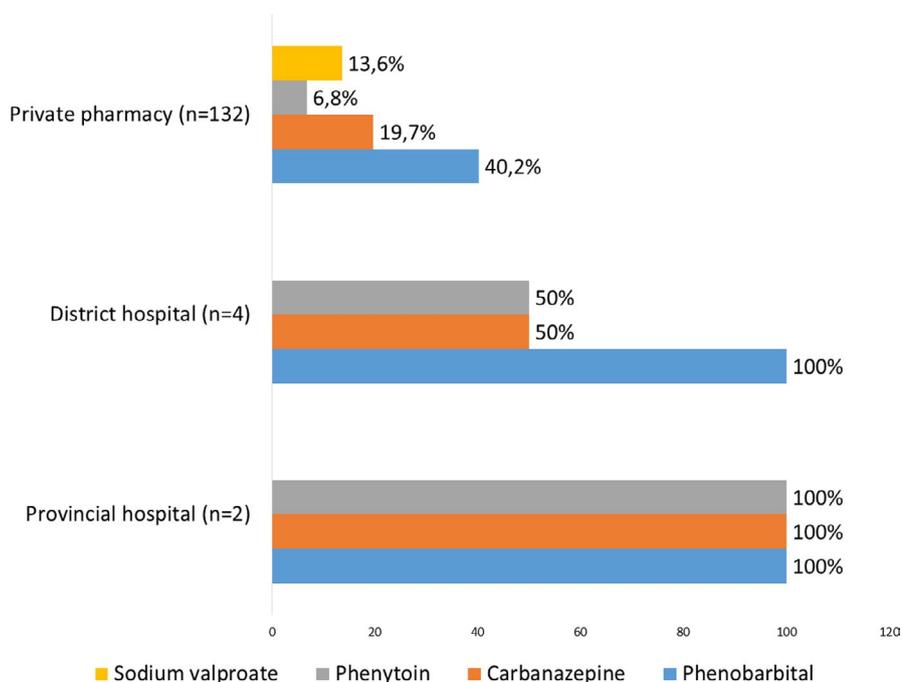


FIGURE 3 Availability of each anti-seizure medication (ASM) within healthcare facilities

available in the public sector was imported from China. Conversely, carbamazepine 200 mg and 400 mg in the private sector were mainly imported from Malaysia (63.3%), and a little from Italy (16.6%), France (13.3%), and Indonesia (3.3%). Phenytoin 100 mg found in the public sector was imported from India, while in the private sector they were imported from Indonesia and the United Kingdom. Sodium valproate 500 mg was imported from France (500 mg and 200 g strengths) and India (only 200 mg strength).

3.3 | Price and affordability of each ASM

Affordability was estimated only in private pharmacies (95.6% from the total of outlets included) because provided free of charge in the public sector. All ASM in private pharmacies was sold at higher prices than the IRP. The lowest MPR was observed for phenobarbital 50 mg with an MPR of 2.1 times higher. The highest MPR was observed for phenobarbital 100 mg with an MPR of 11.3 times higher. But, affordability for phenobarbital 50 mg and 100 mg was the best, with 0.6 and 0.5 days, respectively, for a month of treatment, compared to phenytoin 100 mg (1.8 days) and carbamazepine 200 mg (2.2 days). The worst affordability was found for sodium valproate 500 mg (9.7 days) and 200 mg (10.1 days), and carbamazepine 400 mg (10.8 days). The affordability of each ASM was similar between urban and rural areas.

3.4 | Quality of ASM

A total of 67 samples of ASM, representing 4100 units, were analyzed: 37.3% of phenobarbital, 26.8% of carbamazepine, 22.3% of sodium valproate, 13.4% of phenytoin. These ASM samples were collected from 39 outlets (25 outlets from urban and 14 outlets from rural areas). The information on all samples collected is detailed in Table 1.

3.4.1 | Packaging and leaflet

A proportion of 17.9% (8/67) of samples were sold without their packaging and leaflet. A leaflet written in both French and Cambodian was found only for local production of phenobarbital 50 mg and 100 mg. For all other ASM, the language used was that of the country of manufacture and in English.

3.4.2 | Drug quality

No sample was identified as counterfeit. Overall, 23.9% [95% CI 14.3-35.9] were substandard (meaning that one test of

the monography failed) (Table S1 to S4). Phenytoin (33.3% [95% CI 7.5-70.1]) had the highest proportion of substandard quality samples, followed by carbamazepine (27.8% [95% CI 9.7-53.5]), phenobarbital (20.0% [95% CI 6.8-40.7]), and sodium valproate (20.0% [95% CI 4.3-48.1]). These substandard samples failed mainly due to AI content. No samples were classified as poor quality (at least two tests failed). A significant difference in substandard samples was observed across healthcare sectors: 31.3% in public vs. 68.8% in private; $P = .016$, but no statistical difference was observed across study areas (urban vs. rural). Figure 4 shows details of the quality in terms of authorized and unlicensed ASM samples.

Samples with a marketing authorization represented 85.1% (57/67) of samples. The good-quality ASM was from all samples imported from France (9 samples), Indonesia (5 samples), China (3 samples), and Spain (3 samples). Substandard were found in 13.0% (3/23) of samples from local production, 50.0% (3/6) from Malaysia, 100.0% (8/8) from India. Among the samples without marketing authorization (14.9%), substandard were found in 66.6% (2/3) of the samples manufactured in Malaysia, in 20.0% (1/5) manufactured in Italy.

3.4.3 | Storage condition

A proportion of 20.5% (8/39) of outlets had an air-conditioning in the storage location, but turned-on only during the opening period in 62.5% (5/8). ASM was exposed to direct sunlight in 46.1% (18/39) and to wind in 53.8% (21/39). Three variables were found to be significantly correlated with the quality of medicine in the univariate analysis. In the final multivariate logistic regression analysis, no significant associated factors were found. These factors were as follows: (i) samples collected in urban areas (univariate, OR 0.26, 95%CI [0.07-0.96], $P = .04$; multivariate, aOR 3.18, 95%CI [0.64-15.80], $P = .1$); (ii) the public sector (OR 7.23, 95%CI [1.50-35.10], $P = .01$; aOR 0.31, 95%CI [0.04-2.02], $P = .2$); (iii) imported products (OR 2.79, 95%CI [0.70-11.06], $P = .1$; aOR 0.38, 95%CI [0.07-1.84], $P = .2$).

4 | DISCUSSION

Cambodia is facing an epidemiological transition with the rise of noncommunicable diseases (NCDs), but the health system's capacity to address NCDs is still insufficient.³¹ Several studies on prevalence, associated factors, stigma, and quality of life related to epilepsy have been conducted in Cambodia since 2011,^{15, 16} but access to epilepsy treatment has not yet been assessed in this country. The present study revealed that access to treatment is an important issue mainly due to the low availability of ASM (less than 36.0%) and

TABLE 1 Information of anti-seizure medication (ASM) sample collected from Cambodia

	Number of samples		Brand name	Dosage form	Number of tablet collection	Fabrication country	Registration (authorization sticker present on the medicine box)	Packaging
	Total	Public						
Urban area								
Phenobarbital								
50 mg	6	1	Phenobarbital	Tablet	20	India	Registered	Available
100 mg	12	5	Phenobarbital	Tablet	420	Local production	Registered	Available
		12	Phenobarbital	Tablet	1120	Local production	Registered	Available
Carbamazepine								
200 mg	13	1	Carbamazepine	Tablet	20	China	Registered	Available
		7	Carzepin	Tablet	580	Malaysia	Only 5 samples were registered	Available
		4	Tegretol 200	Tablet	110	Italy	Nonregistration	Available
		1	Bamgetol 200	Tablet	20	Indonesia	Registered	Available
400 mg	1	1	Tegretol	Slow-release tablets	20	Italy	Nonregistered	Available
Phenytoin								
100 mg	3	1	Phenytoin	Tablet	20	India	Registered	Available
		1	Di-Hydan	Tablet	20	United Kingdom	Nonregistered	Available
		1	Kutoin 100	Capsule	20	Indonesia	Registered	Available
Sodium valproate								
200 mg	6	3	Valparin	Enteric coated tablet	260	India	Registered	Available
		3	Depakine	Gastro-resistant tablet	120	Spain	Registered	Available
500 mg	9	9	Depakine Chrono	Prolonged release tablets	290	France	Registered	Available
Rural area								
Phenobarbital								
50 mg	1	1	Phenobarbital	Tablet	20	India	Registered	Available
100 mg	6	6	Phenobarbital	Tablet	520	local production	Registered	Available
Carbamazepine								
200 mg	4	2	Carbamazepine	Tablet	40	China	Registered	Available
		2	Carzepin	Tablet	80	Malaysia	Only 1 sample was registered	Available

(Continues)

TABLE 1 (Continued)

	Number of samples			Dosage form	Number of tablet collection	Fabrication country	Registration (authorization sticker present on the medicine box)	Packaging
	Total	Public	Private					
Phenytoin 100 mg	6	2		Tablet	40	India	Registered	Available
			1	Tablet	60	United Kingdom	Nonregistered	Available
			3	Capsule	300	Indonesia	Registered	Available
Total	67	9	58		4100			

quality issues (20.0%–33.3%). Poor availability of medicine is widely recognized as an important barrier toward reaching optimal treatment.^{32,33} Several elements contribute to the low availability of ASM in Cambodia. First, the number of facilities offering mental health services (including epilepsy) is limited, which exacerbates diagnostic problems.¹⁷ Secondly, the lack of financial resources allocated to the mental health sector leads to a shortage of medications including ASM.³⁴ Lastly, the distribution of ASM is of little interest to pharmaceutical companies due to the low market volume.³⁵ The low availability of ASM seems to be one of the important factors concerning the high rate of patient treated with traditional medicine in Cambodia.³⁴

The availability found in our study was lower than previous studies in other border countries such as Vietnam (>36.0% for carbamazepine and phenytoin)³⁶ and Thailand (above 80%).^{37, 38} In contrast, we found a higher availability and better affordability than a recent study in Lao PDR, conducted over the same period with the same methodology, and reported availability of less than 15.0%.⁸ This difference could be partly explained by the type of facilities considered. In the present study, we included provincial/district hospitals and private pharmacies, which are the main providers of treatments in the whole supply chain of Cambodia, whereas in Lao PDR all types of facilities were considered. Three local pharmaceutical manufacturers provide local production of phenobarbital in Cambodia, and we found a greater proportion of imported ASM than in Lao PDR. The importation of ASM in Lao PDR was limited, mainly from Thailand and Vietnam, and there is only one source of phenobarbital, provided by a local manufacturer. On the other hand, 85% of the Cambodian population considers epilepsy as a treatable disease, consistent with adherence to chronic treatment,³⁹ the situation in Laos is different.⁴⁰ In terms of quality, the proportion of substandard ASM in Cambodia (23.9%) was higher and concerned all ASM available, than that observed in Lao PDR (15.0%),⁸ concerning only local phenobarbital. The proportion of substandard found in this study (23.9%) was higher than in the previous study in Mauritania (13.7%)⁴¹ but lower than a study in Vietnam (65.0%)¹⁰ and sub-Saharan Africa (32.3%).¹¹ Most of the substandard found in Cambodia were from India and Malaysia. There are about 20 000 manufacturers in India that produce and supply low-cost pharmaceuticals products.⁴² WHO has pointed out India as the largest producer of counterfeit and substandard medicines in Asia, and 75% of the world's substandard medicines come from India.⁴³ In Cambodia, among the 300 importing companies (wholesaler), 60% are Indian.⁴⁴ This situation may facilitate the importation of low-quality medicines, not only for ASM but for all medicines. Similarly, no association between storage conditions and substandard quality was observed. Insufficient quality control and/or lack of compliance during the manufacturing process may be the source of these

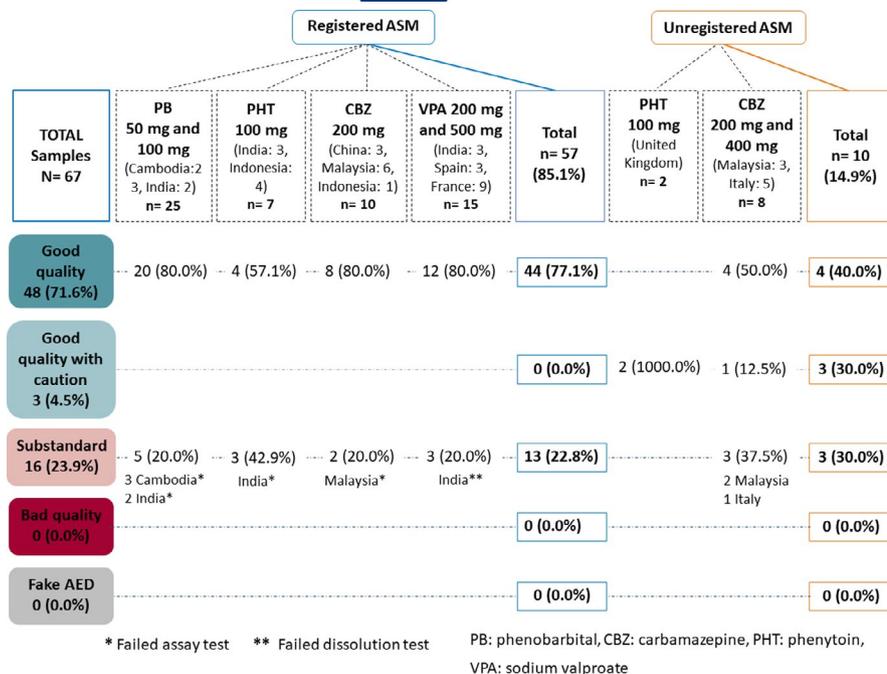


FIGURE 4 Quality of all anti-seizure medication (ASM) samples

substandard. Cross-border trade flows do not appear to interfere with official drug supply channels in Cambodia, as no ASM was imported from border countries.

The availability in both public and private sectors, found in our study, was better compared to a study conducted in 40 countries in 2011,⁴⁵ with a proportion of 29.4% in the public sector and 40.3% in the private sector. Although there was good availability and no charge for ASM in public sector facilities, it was only limited to provincial and district hospitals. The indirect costs and other factors such as distance, lack of transportation, loss of work can be barriers to regular treatment. We emphasized that more than 68.0% of poor-quality samples available in the private sector are leading to a loss of confidence in the healthcare system. As the previous study had reported that only 15.0% of the Cambodian population seek their treatment at a public institution, while 78.0% went to private clinics and pharmacies, even patients had an important part of out-of-pocket.^{14, 46, 47} The affordability found in our study was better than study in Malawi⁴⁸ which require more than 5 days of work. Affordability of sodium valproate was similar to affordability reported in Malawi (>10 days of work) but higher than the of Cameroon countries (7.7 days of work) and in Siri Lanka⁴⁹ (4.7 days of work).

This study has strengths and weaknesses. The main limitation is that we did not investigate the procurement price in each healthcare facility. The availability of ASM at the time of data collection may not be the same throughout the year. Besides, our measure of affordability did not consider other diagnostic or consultation costs and other indirect costs such as transportation cost and loss of day work. The main strength of this study is its multicentric design, providing a picture of socio-economically different areas. Availability

and price were assessed in real-life situations by acting as patients for data collection, and quality analysis was consistent with standard international methodologies.

Increasing and assuring domestic production of ASM is an integral part of the strategy to lower drug prices and increase availability. This is one of the long-term and sustainable strategies that will directly affect economic development. The cost of epilepsy treatment could be reduced by making epilepsy care completely local or by distributing at least ASM monthly at specific points in community-based facilities.^{50, 51}

5 | CONCLUSION

People in developing countries account for about 80% of the world's population but only about 20% of global drug sales. An imbalance between needs, medical potential, and actual availability of medicines has led to issues and poor health outcomes.⁵² In our study, we found a lack of access to affordable ASM due to their low availability. Moreover, among available and affordable ASM, one in five was of poor quality. For this phenomenon, our research highlights the need for future policy efforts to improve the availability of ASM with quality assured, which is currently known as the most important strategy to reduce mortality and disability due to epilepsy. The Cambodian government must improve and guarantee patients' access to diagnosis in health services, particularly in primary healthcare services, and revise the evaluation of their annual needs for these medicines. In addition, the local production of ASM should be strengthened and supported to ensure a controlled and

constant supply. Concerning the importation, a rise of bidding for a public tender procedure would enhance identification of relevant and reliable suppliers. A change in policy should be done to ensure that the drug market policy is not guided predominantly by the purchase price, but also by commitments to both quality and supply. The reinforcement of analytical and control capacities of the pharmaceutical market is also to be foreseen. This is an important step in reducing the treatment gap by ensuring a constant availability of qualitative medicines.

CONFLICT OF INTEREST

The authors confirm that there is no conflict of interest. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

ORCID

Noudy Sengxeu  <https://orcid.org/0000-0002-5715-2051>

Jeremy Jost  <https://orcid.org/0000-0001-5543-3741>

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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